## REMARKS

Applicant acknowledges with appreciation the withdrawal of the restriction requirement, as well as the indication in the Office Action that claims 11-22, 30, 40 and 41 are allowed.

**With respect to the objections to the specification**, submitted herewith is an abstract of the disclosure. In addition, as requested by the Examiner, the specification has been reviewed in order to determine the presence of and remedy minor errors, and as a result this paper incorporates several amendments to the specification to insert headings where appropriate. The amendment at page 9 to insert the heading "Description of the Drawings" before the description of the figures in the application is believed to make it clearer that the specification contains a description of the figures, as requested by the Office Action.

**Claim 25 stands rejected under 35 U.S.C.§ 112, second paragraph**, as indefinite due to the recitation in line 1 "wherein the phosphine is selected from" a group of certain compounds in the Office Action. The Office Action alleges that the claim lists in the group of compounds one that is not a phosphine. This rejection has been carefully considered, and is respectfully traversed because all of the recited group members are indeed phosphines. The compound "dibenzyl-N,N-diethylphosphoramidite" is in fact a phosphine, and this compound can also properly be named "dibenzyl(N,N-diethylamido)phosphine". The nomenclature used in the rejected claim is used in the specification. Accordingly, reconsideration and withdrawal of the rejection of claim 25 under 35 U.S.C.§ 112, second paragraph is most respectfully requested.

**Claims 23, 24 and 26-29 stand rejected under 35 U.S.C. § 102(b) as anticipated by Rathbone et al. (WO92/16486).** These claims have been amended to delete from step (b) the use of "an acidic compound" to contact the protected phosphate ester of Formula I. Rathbone fails to disclosure each and every limitation of the presently claimed method for preparing compound III using the steps, regents, conditions, etc. required by claim 23 and claims dependent thereon. Thus, withdrawal of the rejection of claim 23 and claims 24 and 26-29 (which depend from claim 23) under 35 U.S.C. § 102(b) is most respectfully requested.

**Claims 33-35 and 37 stand rejected under 35 U.S.C. § 102(b) as anticipated by Pettit '122 (U.S. Patent No. 5,561,122).** These claims have been amended to clarify that "Q" cannot be sodium or potassium. Pettit '122 fails to disclose the compounds or compositions set forth in the recited claims. Accordingly, withdrawal of this rejection is respectfully requested.

**Claims 31-38 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Pettit '122 in view of Hochlowski '799 (U.S. Patent No. 5,484,799).** The Office Action urges that Pettit '122's teaching of the formation of disodium and dipotassium combretastatin A-4 3'-0-phosphate from the corresponding ammonium hydrogen salt renders the claimed invention obvious to one of ordinary skill in the art. The Office Action further alleges that it would have been obvious to one of ordinary skill in the art to directly form it from the diacid, and acknowledges that Pettit '122 does not suggest alkali metal salts other than sodium and potassium. However, the Office Action alleges that Hochlowski '799 teaches that, for

pharmaceutical purposes, lithium, potassium, sodium, calcium, magnesium and ammonium salts are equivalent.

The position taken in the Office Action has been carefully considered, and is most respectfully traversed and requested to be withdrawn. Despite the urging in the Office Action, there is no motivation in either Pettit '122 or Hochlowski '799, whether taken alone or in combination to achieve the claimed invention. Moreover, there is simply no suggestion in either reference which would motivate one of skill to consider the teachings of these respective references.

Pettit '122 contains no suggestion or motivation to make a salt other than the sodium or potassium salt. The respective compounds of Pettit '122 and Hochlowski '799 are totally unrelated compounds, both structurally and via mechanism of action. Combretastatin binds to tubulin, and Hochlowski '799's compounds do not. Given two totally different mechanisms of action, one of skill would not try to modify Pettit by substituting with salts taught in the other reference. Moreover, different salts tend to be of varying sizes and properties, such that one cannot simply substitute one for another, from one compound to the next. For example, different types of salts have different dissolution rates, different degrees of solubilization, different surface activity, different stability in the physiological environment, different toxicity characteristics, etc., depending upon the size and type of the salt-forming molecule.

Thus, it is not correct to say that one of skill in the art would find motivation to combine Pettit '122 with Hochlowski '799. Therefore, withdrawal of the rejection of Claims 31-38 under 35 U.S.C. § 103(a) is earnestly solicited.

Claim 39 has been objected to as being dependent upon a rejected base claim, and the Office Action states that claim 39 would be allowable if rewritten in independent form to include all the limitation of the base claim. The foregoing arguments are believed to render moot this objection.

In view of the foregoing, favorable consideration and allowance of the claims is most respectfully requested. The Examiner is invited to telephone the undersigned, if he believes that this would in any way facilitate prosecution of this application.

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Respectfully submitted,

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